PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS (PREPARATIONS) 1986

This medicine is to be supplied upon physician's prescription only

ZINPLAVA® 25 mg/mL
Concentrate for Solution for Infusion

Each mL of concentrate contains:
25 mg of bezlotoxumab
For a list of inactive ingredients see section 6. "FURTHER INFORMATION". See also section 2.7 "Important information about some of the ingredients of the medicine".

Read all of this leaflet carefully before using this medicine.
- This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

1. WHAT ZINPLAVA IS INTENDED FOR?

ZINPLAVA is a medicine that is given together with an antibiotic to prevent *Clostridium difficile* infection (CDI) from coming back in patients 18 years of age or older who have a high risk of CDI coming back.

Therapeutic group: Antiinfectives for systemic use, specific immunoglobulins.

How ZINPLAVA works
- When people get CDI, they are usually given an antibiotic to get rid of the infection, but CDI can come back within weeks or months.
- The bacteria responsible for CDI produce a toxin that can inflame and damage your colon, causing stomach pain and severe diarrhoea. **ZINPLAVA** acts by attaching to the toxin and blocking it, thereby preventing the symptoms of CDI from coming back.

2. BEFORE USING ZINPLAVA

Talk to your doctor before you are given **ZINPLAVA**.

2.1 Do not use ZINPLAVA if:

you are hypersensitive (allergic) to bezlotoxumab or any of the other ingredients of this medicine (For a list of inactive ingredients, see section 6).

2.2 Special warnings regarding use of ZINPLAVA
ZINPLAVA is not a treatment for CDI. **ZINPLAVA** has no effect on the CDI you have now.

ZINPLAVA is given with the antibiotic therapy you are taking for CDI.

2.3 Children and adolescents
ZINPLAVA should not be used in children and adolescents below 18 years of age.
There is no data available regarding the safety and efficacy of the medicine in children and adolescents.

2.4 Interactions with other medicines
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, you should tell the doctor or pharmacist.

2.5 Pregnancy and breast-feeding
- If you are pregnant or trying to get pregnant, tell your doctor.
- We don't know if **ZINPLAVA** will harm your baby while you are pregnant.
- If you are breast-feeding or are planning to breast-feed, check with your doctor first.
- We don't know if **ZINPLAVA** gets in your breast milk and is passed to your baby.
- You and your doctor should decide together if you will use **ZINPLAVA**.

2.6 Driving and using machines
ZINPLAVA has no or very little effect on the ability to drive and use machines.

2.7 Important information about some of the ingredients of the medicine
Each mL of concentrate contains 0.2 mmol (4.57 mg) sodium.

3. HOW SHOULD YOU USE ZINPLAVA?

Always use the medicine as instructed by the doctor.
You should check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.
The dosage and treatment regimen will be determined by the doctor only.

- You will get **ZINPLAVA** as an infusion (drip) into a vein.
- You will get **ZINPLAVA** in one dose and it will take about 1 hour. Your dose will be calculated using your body weight.
- You should keep taking your antibiotic for CDI as directed by your doctor.

Do not exceed the recommended dose.

If you miss an appointment to get ZINPLAVA
- Call your doctor or health care professional right away to reschedule your appointment.
- It is very important that you do not miss the dose of this medicine.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have any further questions on the use of this medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, **ZINPLAVA** may cause side effects, in some patients.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

The following side effects have been reported in clinical trials:

Common side effects (may affect up to 1 in 10 people)
- diarrhoea
- dizziness
- feeling sick (nausea)
- fever
- headache
- high blood pressure
- shortness of breath
- tiredness

Tell your doctor or health care professional if you notice any of the side effects above.
If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Reporting of side effects
Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store ZINPLAVA?

- Avoid Poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use this medicine after the expiry date (exp. date) which is stated on the carton and vial label. The expiry date refers to the last day of the indicated month.
- **Storage conditions**: Store in a refrigerator 2°C to 8°C. Do not freeze. Keep vial in the outer carton in order to protect from light.
  The diluted solution of **ZINPLAVA** may be stored either at room temperature (at or below 25°C) for up to 16 hours or under refrigeration at 2°C to 8°C for up to 24 hours. These time limits include the duration of infusion. From a microbiological point of view, the product must be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and must not be longer than 24 hours at 2°C – 8°C or 16 hours at room temperature (at or below 25°C). If refrigerated, allow the IV bag to come to room temperature prior to use.
- Do not store any unused portion of the infusion solution for reuse. Any unused medicine or waste material should be disposed of as instructed by your doctor or pharmacist.

6. FURTHER INFORMATION

What ZINPLAVA contains
In addition to the active ingredient **ZINPLAVA** also contains:
Sodium chloride, sodium citrate dihydrate, citric acid monohydrate, polysorbate 80, diethylenetriaminepentaacetic acid, water for injections and sodium hydroxide (for pH adjustment).

What ZINPLAVA looks like and contents of the pack
The concentrate for solution for infusion is a clear to moderately opalescent, colourless to pale yellow liquid.
Pack size: A carton containing one glass vial.

Marketing Authorization Holder and Address:
Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O.Box 7121, Petah-Tikva 49170.

Manufacturer:
Merck Sharp & Dohme Corp., New-Jersey, USA.

This Leaflet was checked and approved by the Ministry of Health in January 2019.

Registration number of the medicine listed in the National Drug Registry of the Ministry of Health: 161-24-35464

The following information is intended for healthcare professionals only:

Preparation of diluted solution

- Prepare the diluted solution immediately after removal of the vial(s) from refrigerated storage, or the vial(s) may be stored at room temperature protected from light for up to 24 hours prior to preparation of the diluted solution.
- Inspect vial contents for discoloration and particulate matter prior to dilution. **ZINPLAVA** is a clear to moderately opalescent, colourless to pale yellow liquid. Do not use the vial if the solution is discoloured or contains visible particles.
- Do not shake the vial.
- Withdraw the required volume from the vial(s) based on the patient's weight (in kg) and transfer into an IV bag containing either 0.9 % Sodium Chloride Injection, or 5 % Dextrose Injection, to prepare a diluted solution with a final concentration ranging from 1 to 10 mg/mL. Mix diluted solution by gentle inversion.
- Discard vial(s) and all unused contents.
- If the diluted solution is refrigerated, allow the IV bag to come to room temperature prior to use.
- Do not freeze the diluted solution.

Method of administration

- Administer the diluted solution for infusion intravenously over 60 minutes using a sterile, non-pyrogenic, low-protein binding 0.2 micron to 5 micron in-line or add-on filter. **ZINPLAVA** should not be administered as an intravenous push or bolus.
- The diluted solution can be infused via a central line or peripheral catheter.
- **ZINPLAVA** must not be co-administered with other medicinal products simultaneously through the same infusion line.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.